Present Claims 1-3 and 5-19 relate to an isolated coryneform bacterium in which L-arginine biosynthesis is not repressed by an *argR* gene in a normal manner, and which has L-arginine producing ability. The inventors have surprisingly found that the presently claimed bacteria are especially useful for producing L-arginine.

The rejection of Claims 1-3 under 35 U.S.C. § 101 as being directed toward non-statutory subject matter has been obviated by appropriate amendment. As the Examiner will note, Claim 1 has been amended to replace "A coryneform bacterium" with "An isolated coryneform bacterium." Accordingly, the rejection is no longer tenable and should be withdrawn.

The rejection of Claims 1-3 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. In the Official Action, the position is taken that Claims 1-3 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. However, Applicants would like to direct the Examiner's attention to the following points.

Some *argR* genes of coryneform bacteria were well known and available at the time the application was filed. For example, the *argR* gene of *Corynebacterium glutamicum* was registered in Genbank as accession No. AF041436. The nucleotide sequence of an *argR* gene for *Mycobacterium tuberculosis* was disclosed in Nature, vol. 393, p. 537 (1998). In this regard, Table III-4-1 of Identification Manual of Actinomycetes (published by Business Center for Academic Societies Japan) (copy attached as Exhibit A) shows that *Mycobacterium* belongs to the same suborder as *Corynebacterium*.

It had not been known whether a protein encoded by *argR* gene actually functions as a repressor of L-arginine biosynthetic system in coryneform bacteria. However, the inventors of the present invention have now discovered, for the first time, an *argR* gene in *Brevibacterium flavum,* which belongs to coryneform bacteria. Therefore, other coryneform bacteria are also reasonably now expected to have *argR* genes, and proteins encoded by *argR* genes are reasonably expected to function as a repressor of the L-arginine biosynthetic system. Consequently, Applicants submit that the specification also provides sufficient enablement for the claimed invention even in such cases when using *argR* gene other than that of *B. flavum.*

For these reasons, the rejection should be withdrawn.

The rejection of Claims 1-3 under 35 U.S.C. §112, second paragraph, has been obviated by appropriate amendment. In particular, Claims 1 and 2 have been amended by replacing "arginine repressor does not function in a normal manner" with "L-arginine biosynthesis is not repressed by an *argR* gene in a normal manner."

Claim 2 has also been amended to replace "a gene coding for the arginine repressor" with "the *argR* gene which has the nucleotide sequence shown in SEQ ID NO:17 or has such a degree of homology that it should cause homologous recombination with the nucleotide sequence shown in SEQ ID NO:17." As stated above, it is now reasonably expected that other coryneform bacteria than *B. flavum* have *argR* genes. The *argR* genes are expected to have the sequences homologous to the sequence of SEQ ID NO:17. Therefore, Applicants believe that these *argR* genes can be disrupted by homologous recombination and this rejection should be overcome.

Claim 3 has been amended by replacing "an amino acid sequence showing homology to the amino acid sequence" with "an amino acid sequence which is encoded by an *argR* gene having such a degree of homology that it should cause homologous recombination with the *argR* gene coding to the amino acid sequence shown in SEQ ID NO:18."

Accordingly, the rejection is no longer tenable and should be withdrawn.

Applicants expressly state on the record that none of these amendments were made or necessary to distinguish the present claims from the prior art.

Applicants submit that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

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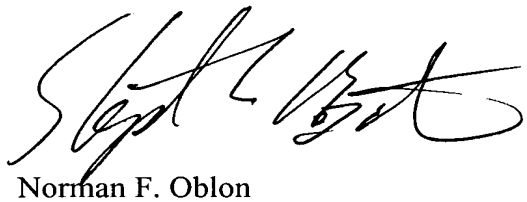

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12-28-01

IN THE CLAIMS

Please amend the claims as follows:

--1. (Amended) [A] An isolated coryneform bacterium in which [an arginine repressor does not function] L-arginine biosynthesis is not repressed by an *argR* gene in a normal manner, and which has L-arginine producing ability.

2. (Amended) The isolated coryneform bacterium according to Claim 1, wherein [the arginine repressor does not function in a normal manner due to disruption of a gene coding for the arginine repressor] L-arginine biosynthesis is not repressed by the *argR* gene in a normal manner due to disruption of the *argR* gene which has the nucleotide sequence shown in SEQ ID NO:17 or has such a degree of homology that it should cause homologous recombination with the nucleotide sequence shown in SEQ ID NO:17, and which is on a chromosome of the bacterium.

3. (Amended) The isolated coryneform bacterium according to Claim 2, wherein the [arginine repressor has] *argR* gene encodes the amino acid sequence shown in SEQ ID NO:18 or an amino acid sequence [showing homology to the amino acid sequence] which is encoded by an *argR* gene having such a degree of homology that it should cause homologous

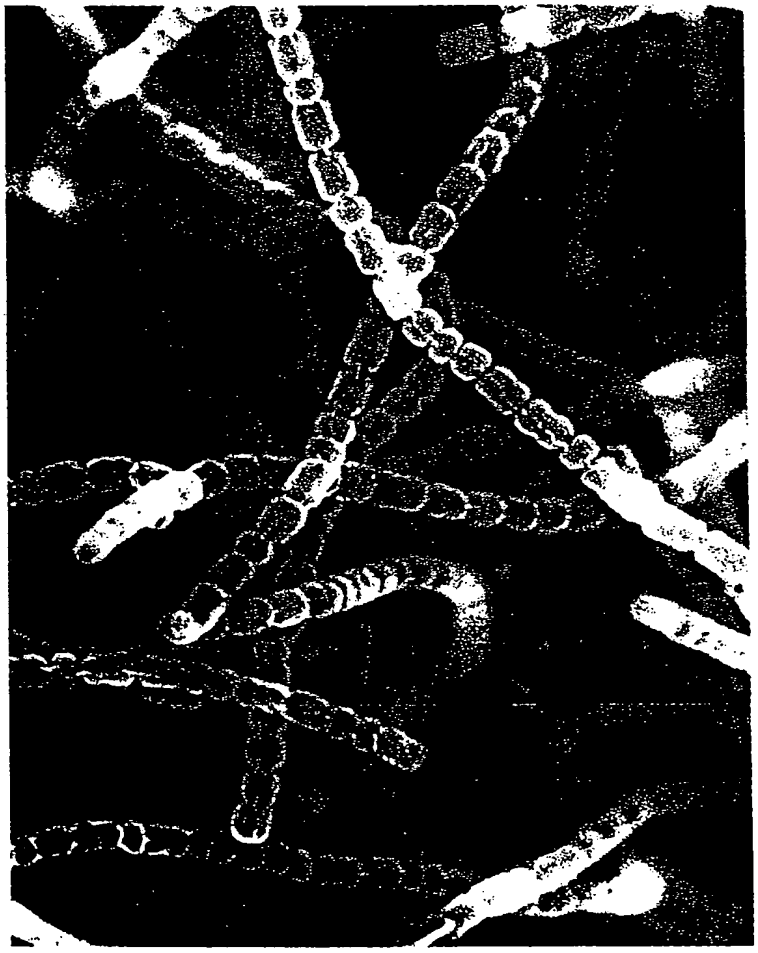
recombination with the *argR* gene coding for the amino acid sequence shown in SEQ ID NO:18.--

Please add the following new claims:

--5. (New) to 19. (New)--

放線菌の分類と同定

日本放線菌学会 編
edited by
The Society for Actinomycetes Japan



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放線菌の分類と同定

日本放線菌学会 編

日本学会事務センター

定価はカバーに表示

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第4章

Family *Corynebacteriaceae* and related families

鈴木健一朗

本菌群は病原菌として古くから知られている結核菌（*Mycobacterium tuberculosis*）やジフテリア菌（*Corynebacterium diphtheriae*）を含み，*Nocardia* 属と合わせて各属の頭文字を取り，CMN グループと呼ばれ，とくに医学細菌学上重要な菌群とされてきた。その後，グルタミン酸生産菌 *Corynebacteirum glutamicum* がこの仲間に入り，アミノ酸発酵の主役となると，産業微生物学的にも注目されるようになり，さらに *Rhodococcus* 属には多くの難分解性人工有機化合物の分解能力が知られるようになって環境微生物学上の重要性も増大した。*Nocardia* 属は生長に伴って断裂する菌糸を持ち，かつては多くの放線菌を形態だけで *Nocardia* と称し，その不均一性が問題となっていたが，1970 年代の化学分類学的研究によって整理され，ほぼ現在の *Nocardia* 属の概念が定着した。そしてミコール酸含有という共通の性質を持つ菌群は 16S rDNA の解析によっても支持され，現在は表 III-4-1 に示す 10 属を数える。これらの各属は 16S rDNA による系統では *Nocardia* と *Rhodococcus* が近縁で同じ科に入るほかは，それぞれほぼ科レベルで分岐している（Rainey *et al.*, 1995, Stackebrandt *et al.*, 1997）。ミコール酸は 2-アルキル 3-ヒドロキシ脂肪酸という一般構造を持つ，分枝ヒドロキシ脂肪酸である。とくに *Mycobacterium* 属のミコール酸はその総炭素数が 90 にも達する特異な脂肪酸で，その炭素数の分布幅は分類群に特徴的である。二重結合数と官能基の有無にも分類群ごとの特徴が見られる（第 II 部第 3 章第 7 節ミコール酸参照）。本章の対象は，Stackebrandt *et al.* (1997) の高次分類群では，order *Actinomycetales* の suborder *Corynebacterineae* に対応する。本菌群の細菌の細胞壁は *meso*-diaminopimelic acid (A_2pm) 直結型のペプチドグリカン (A1γ) と，その外側に arabinose と galactose からなる多糖層を持つ点が共通である。そしてミコール酸はアラビノガラクタンに共有結合し，あるいはトレハロース 6,6′ ジミコール酸のような糖脂質として存在する。この菌群の中にも例外的にミコール酸を持たない分類群も存在する。*Turicella* 属と *Corynebacterium amycolatum* である。他の放線菌群と同様，化学分類学的表現性状と系統分類はよく対応しているが，表現性状だけで属を特定するのが困難な場合もあるので，分類および同定には総合的な判断が求められる。この菌群においてとくに有効な属の識別指標はメナキノンの分子種（Collins *et al.*, 1977）と，グリコリルテストによる細胞壁アシル型，そしてリン脂質とミコール酸である。これらの化学分類学的性状による属の概念を表 III-4-2 に示す。

本菌群の生理・生化学性状は，とくに炭素化合物の資化性が多様で，種の特徴の記載には重要である。臨床株が主体の *Corynebacterium*, *Mycobacterium*, *Turicella* を除き，一般には Gordon の方法（Gordon & Mihm, 1957），または Goodfellow の方法（Goodfellow, 1971）が用いられる。

本菌群は応用分野から臨床分野まで幅広い研究対象となり，人間とのかかわりも多様である。したがって，目的に応じた微生物との接し方があってしかるべきであり，微生物の認識の仕方も様々である。遺伝子解析技術を使った分類体系の構築に対して，同じデータベースを用いた検出手法とは相互に評価して一層価値が高まるものである。医学微生物には重要な目的が含まれている。一般微生物の分類を専門とする立場で本章を執筆しているので，病原放線菌の同定を行うときには医学微生物学の専門書も合わせて参考にして，重要な目的を見失わないようにされることを願うものである。

表 III-4-1. Suborder *Corynebacterineae*

科	属
Corynebacteriaceae	*Corynebacterium*
	Turicella
Dietziaceae	*Dietzia*
Gordoniaceae	*Gordonia*
Mycobacteriaceae	*Mycobacterium*
Nocardiaceae	*Nocardia*
	Rhodococcus
Tsukamurellaceae	*Tsukamurella*
帰属不明	*Skermania*
	Williamsia

Corynebacterium 属

本属は基準種 *C. diphtheriae* に代表される多くの人畜病